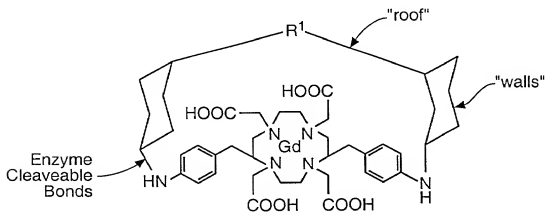
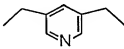
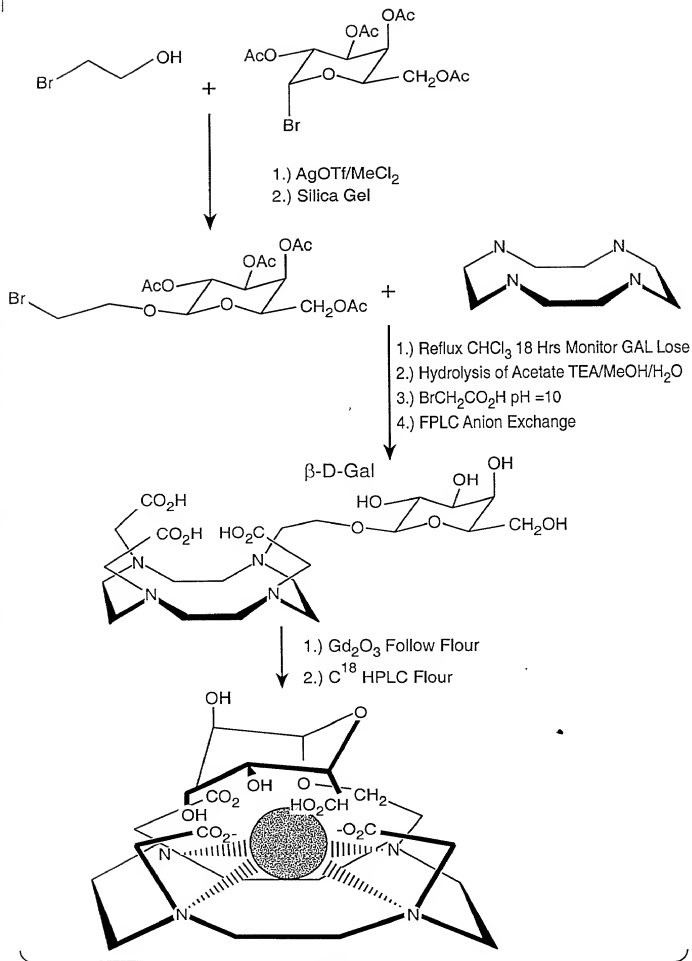
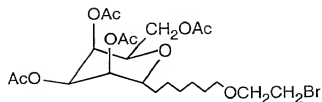
Where R¹**FIG. 1**Where R¹**FIG. 2**

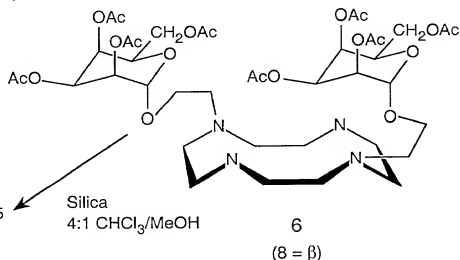
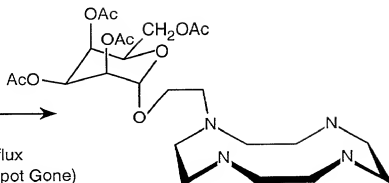
09066512-052401





1 + 2

CHCl_3
 48 Hrs Reflux
 T.L.C. (2 Spot Gone)



8

- 1.) Hydrolysis Of Acetate
TCA/MeOH / H_2O
- 2.) $\text{BrCH}_2\text{CO}_2\text{H}$ pH = 10
- 3.) FPLC Cation Exchange
pH = 2 Acetic Acid Gradient

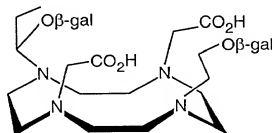
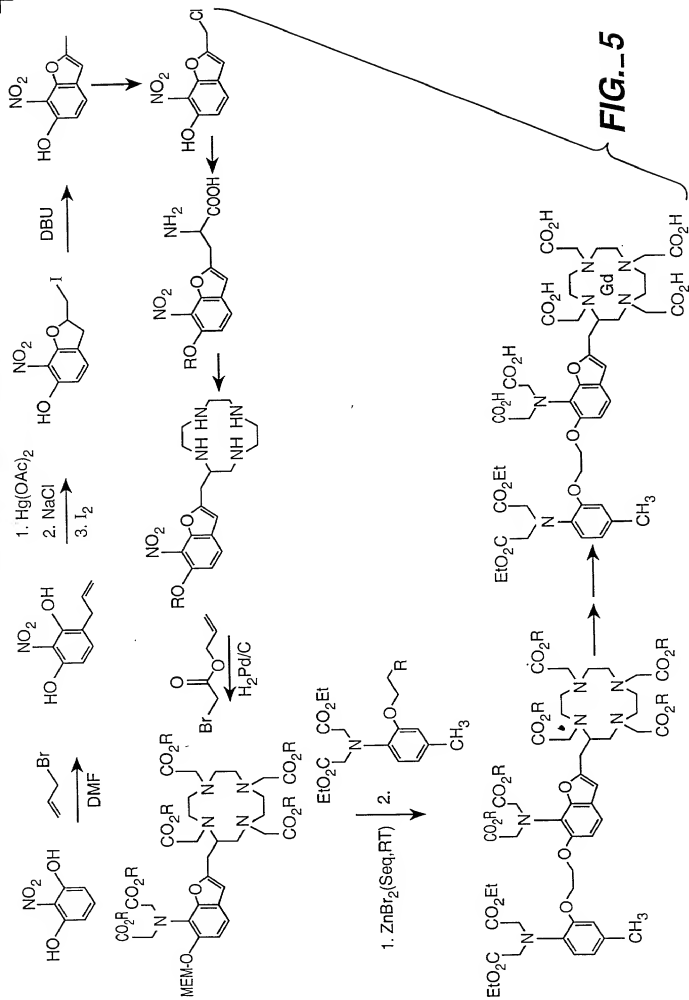
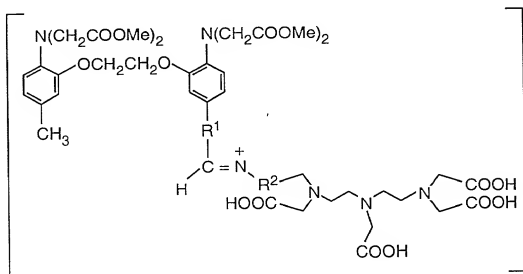
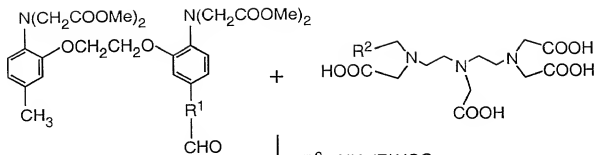


FIG._4





Rearrangement
 HPLC
 Gd(III)

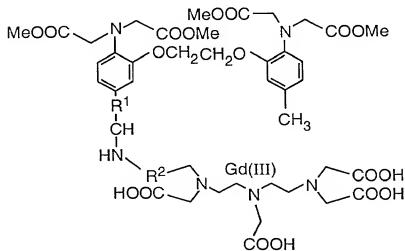
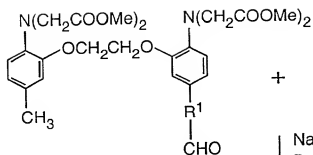


FIG. 7



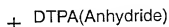
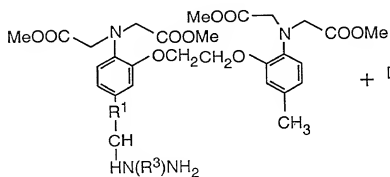
I.



$$\begin{array}{c}
 \downarrow \\
 \text{NaCNBH}_3 \\
 \text{Dry MeOH} \\
 \text{Argon}
 \end{array}$$

$$\downarrow$$

 HPLC



II.

$$\downarrow$$

 HPLC

$$\downarrow$$

 Gd(III)

$$\downarrow$$

 Remove Protecting
 Groups

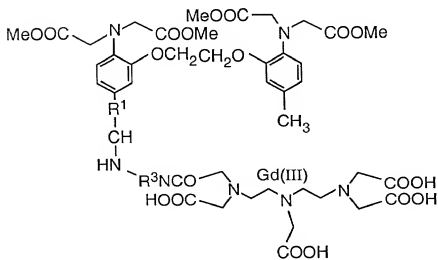


FIG. 8

104250.21599860

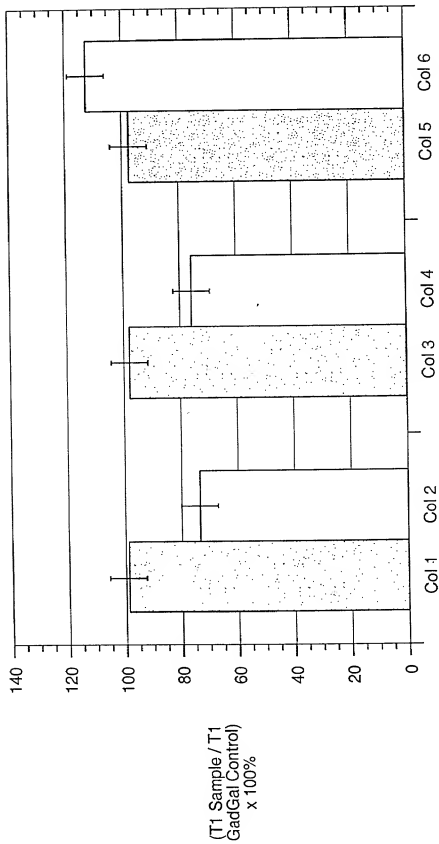
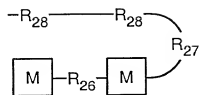
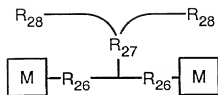
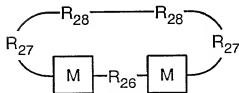
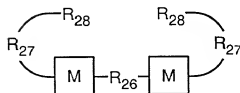
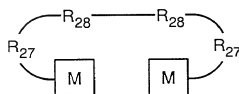
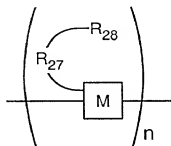
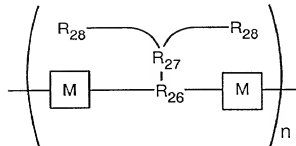
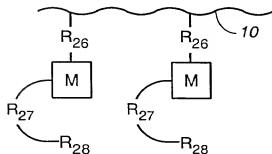
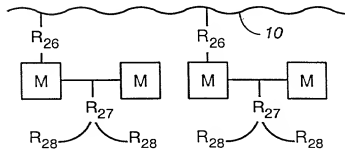
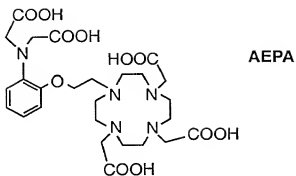


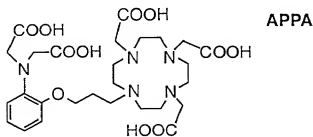
FIG._9

**FIG. 10A****FIG. 10B****FIG. 10C****FIG. 10D****FIG. 10E****FIG. 10F****FIG. 10G****FIG. 10H****FIG. 10I**



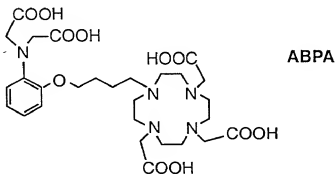
1-o-aminophenoxy-2-(cyclen)ethane-N,N,N',N'',N'''-pentaacetic acid

FIG._ 11A



1-o-aminophenoxy-3-(cyclen)propane-N,N,N',N'',N'''-pentaacetic acid

FIG._ 11B



1-o-aminophenoxy-4-(cyclen)butane-N,N,N',N'',N'''-pentaacetic acid

FIG._ 11C



09866512-052401



FIG. 12



+

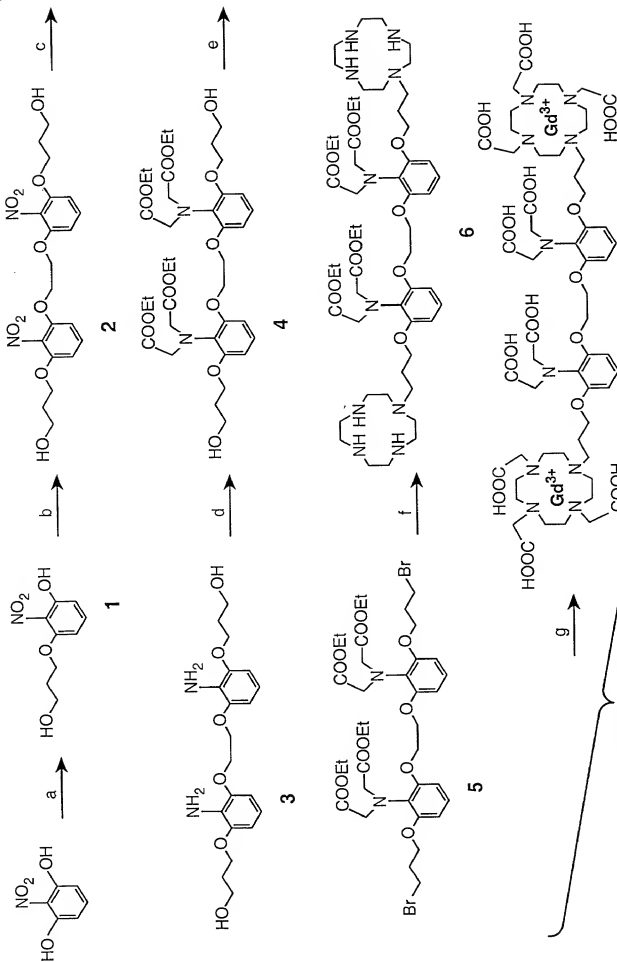


FIG. 14

+

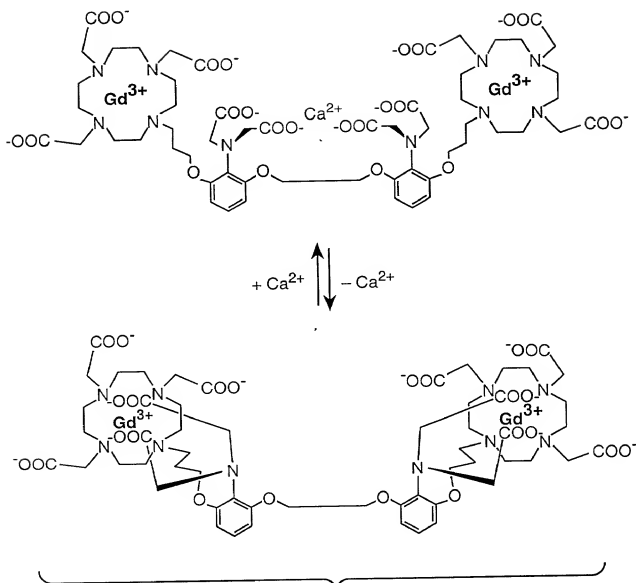


FIG. 15

09866512.052401

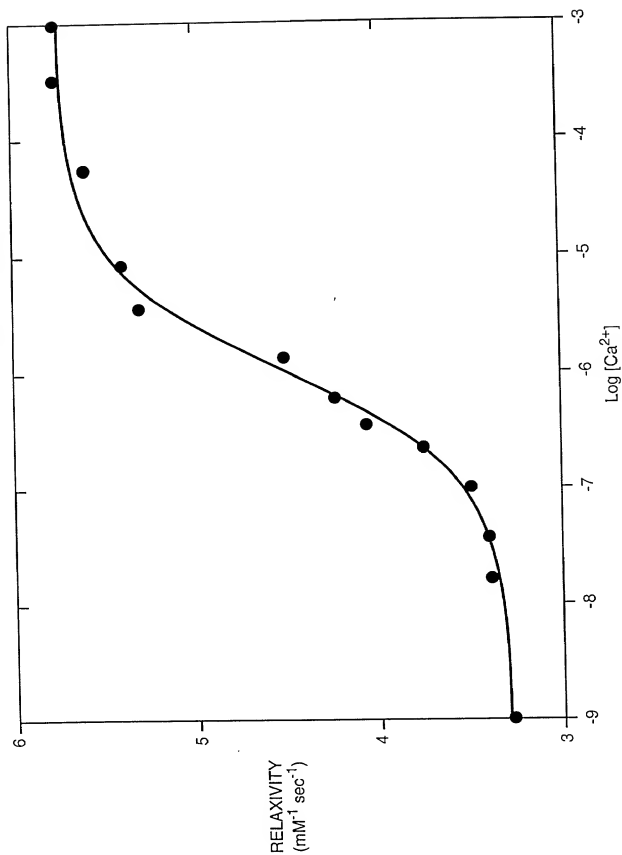


FIG. 16

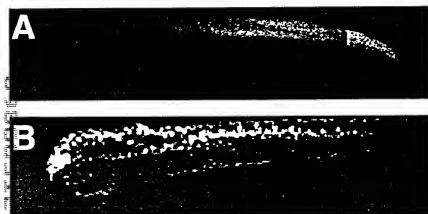


FIG._18

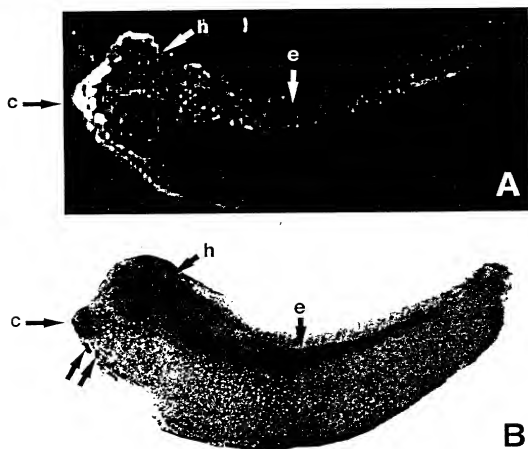


FIG._19

Enzyme Activation

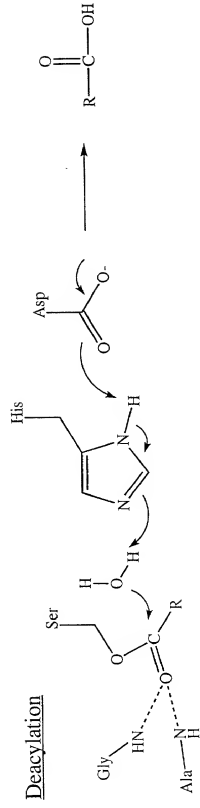
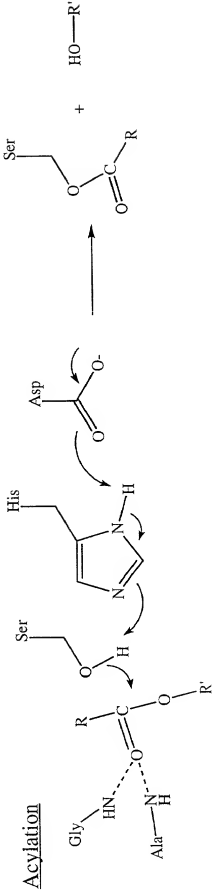
Fig 20A

Properties of Carboxylesterases:

1. Efficient cleavage of Ester functional groups

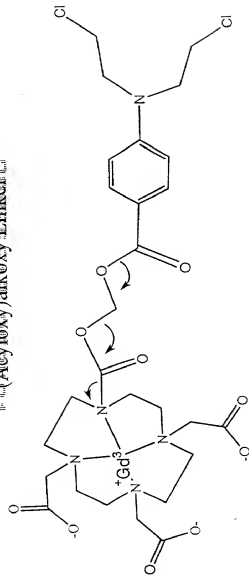


2. Belongs to the family of Ser-His-Asp active site enzymes (serine protease)



TE(Acyloxy)alkoxy Linker

Fig 20A.B



esterase

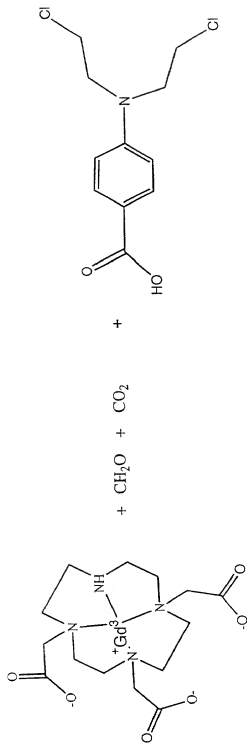
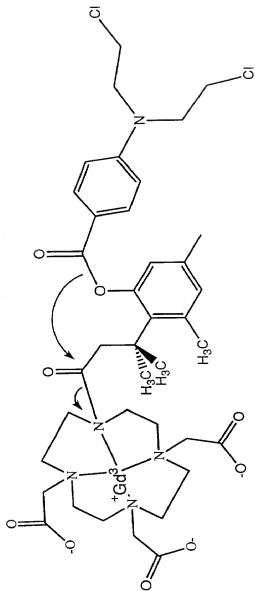
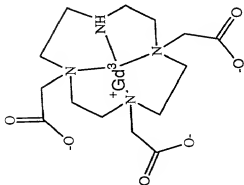


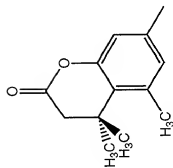
Fig 208C



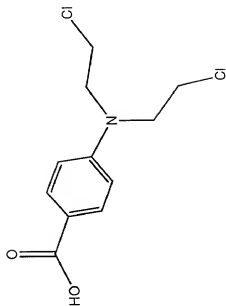
esterase

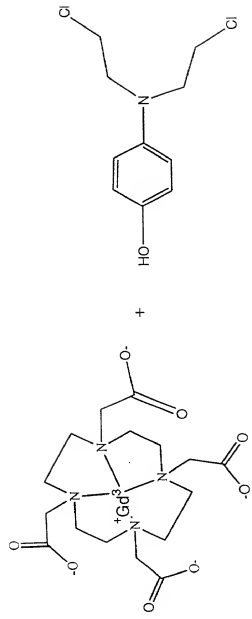
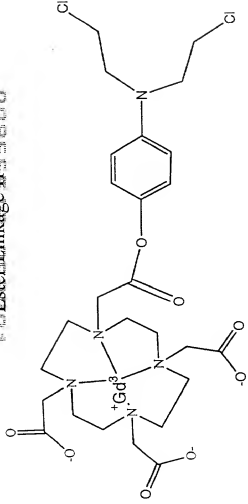


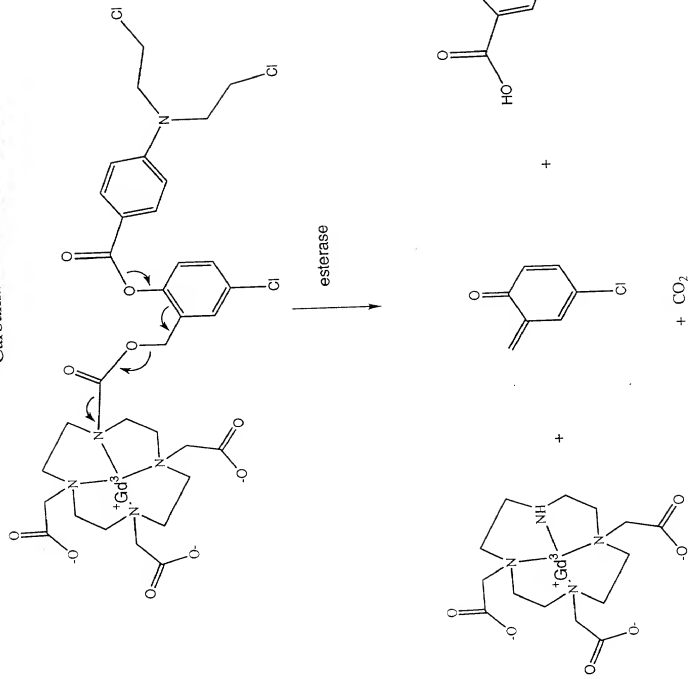
+



+







Fmoc Chemistry for Synthesis of Linker-peptide unit

I.

MBHA Rink Amide Resin

or

PAL-PEG-PS Resin

Activation with 20% piperidine
in DMF

Fmoc-AA-OH/HOAT/HATU/DIEA

1. N-ε-Fmoc-ε-amino-R acid

$[H_2C(CH_2)_x-NH-Fmoc]$

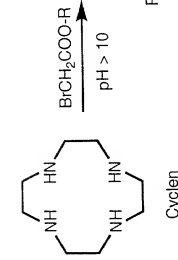
2. Fmoc-AA-OH

3. Fmoc-AA-OH

4. (Fmoc-AA-OH)_n

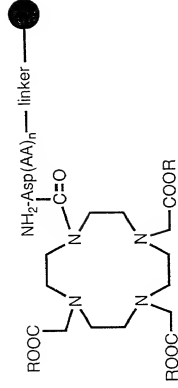
5. Fmoc-Asp-OH

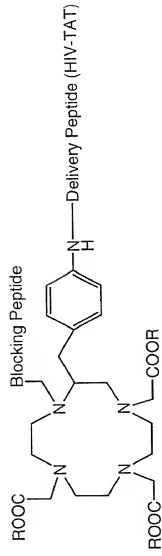
II.



Fmoc-Asp-(AA)_n—linker—●

III.





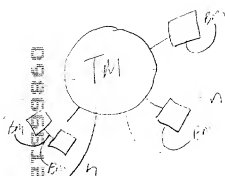
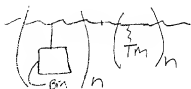
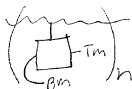
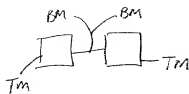
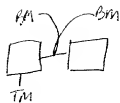
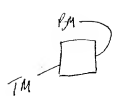


Fig 23